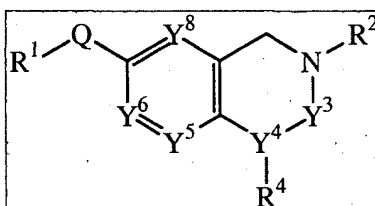


CLAIMS

What is claimed is:

5

1. A compound of Formula I



or a pharmaceutically acceptable salt thereof,
wherein:

10

R¹ is independently selected from:

C₅ or C₆ cycloalkyl-(C₁-C₈ alkylenyl);

Substituted C₅ or C₆ cycloalkyl-(C₁-C₈ alkylenyl);

C₈-C₁₀ bicycloalkyl-(C₁-C₈ alkylenyl);

Substituted C₈-C₁₀ bicycloalkyl-(C₁-C₈ alkylenyl);

15

5- or 6-membered heterocycloalkyl-(C₁-C₈ alkylenyl);

Substituted 5- or 6-membered heterocycloalkyl-(C₁-C₈ alkylenyl);

8- to 10-membered heterobicycloalkyl-(C₁-C₈ alkylenyl);

Substituted 8- to 10-membered heterobicycloalkyl-(C₁-C₈ alkylenyl);

Phenyl-(C₁-C₈ alkylenyl);

20

Substituted phenyl-(C₁-C₈ alkylenyl);

Naphthyl-(C₁-C₈ alkylenyl);

Substituted naphthyl-(C₁-C₈ alkylenyl);

5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);

25

8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);

Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

30

Substituted naphthyl;

5- or 6-membered heteroaryl;
Substituted 5- or 6-membered heteroaryl;
8- to 10-membered heterobiaryl; and
Substituted 8- to 10-membered heterobiaryl;

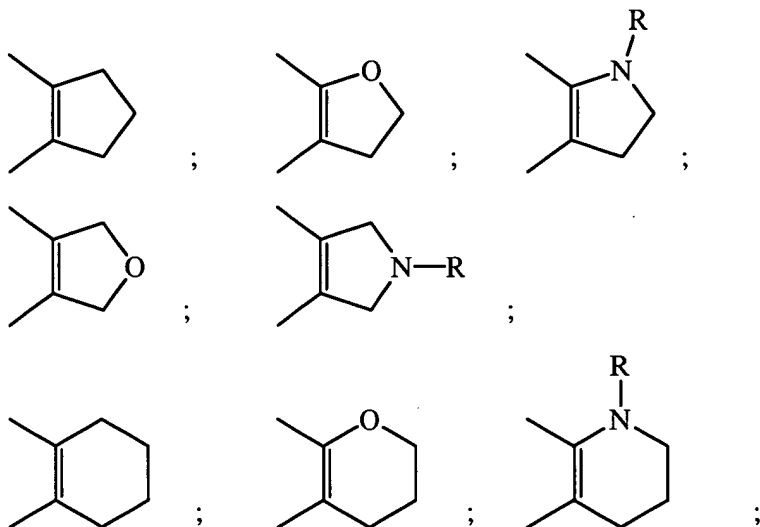
5 R^2 is independently selected from:

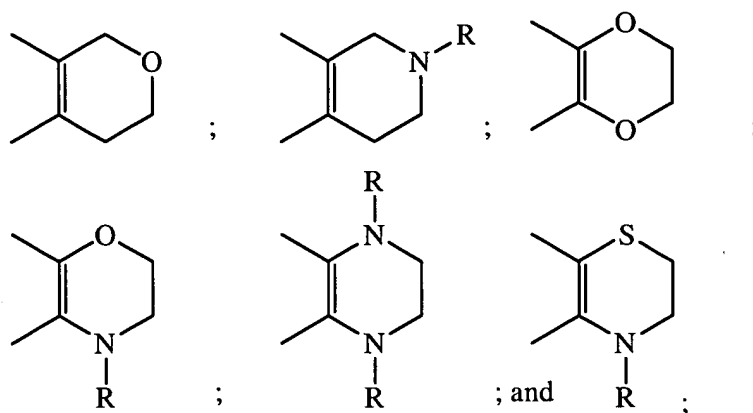
H;
C₁-C₆ alkyl;
Phenyl-(C₁-C₈ alkylenyl);
Substituted phenyl-(C₁-C₈ alkylenyl);
10 Naphthyl-(C₁-C₈ alkylenyl);
Substituted naphthyl-(C₁-C₈ alkylenyl);
5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);
15 Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);
Phenyl-O-(C₁-C₈ alkylenyl);
Substituted phenyl-O-(C₁-C₈ alkylenyl);
Phenyl-S-(C₁-C₈ alkylenyl);
Substituted phenyl-S-(C₁-C₈ alkylenyl);
20 Phenyl-S(O)-(C₁-C₈ alkylenyl);
Substituted phenyl-S(O)-(C₁-C₈ alkylenyl);
Phenyl-S(O)₂-(C₁-C₈ alkylenyl); and
Substituted phenyl-S(O)₂-(C₁-C₈ alkylenyl);

Each substituted R^1 and R^2 group contains from 1 to 4 substituents, each
25 independently on a carbon or nitrogen atom, independently selected from:

C₁-C₆ alkyl;
CN;
CF₃;
HO;
30 (C₁-C₆ alkyl)-O;
(C₁-C₆ alkyl)-S(O)₂;
H₂N;
(C₁-C₆ alkyl)-N(H);

- $(C_1-C_6 \text{ alkyl})_2-N$;
 $(C_1-C_6 \text{ alkyl})-C(O)O-(C_1-C_8 \text{ alkylene})_m$;
 $(C_1-C_6 \text{ alkyl})-C(O)O-(1 \text{ to } 8\text{-membered heteroalkylene})_m$;
 $(C_1-C_6 \text{ alkyl})-C(O)N(H)-(C_1-C_8 \text{ alkylene})_m$;
5 $(C_1-C_6 \text{ alkyl})-C(O)N(H)-(1 \text{ to } 8\text{-membered heteroalkylene})_m$;
 $H_2NS(O)_2-(C_1-C_8 \text{ alkylene})$;
 $(C_1-C_6 \text{ alkyl})-N(H)S(O)_2-(C_1-C_8 \text{ alkylene})_m$;
 $(C_1-C_6 \text{ alkyl})_2-NS(O)_2-(C_1-C_8 \text{ alkylene})_m$;
3- to 6-membered heterocycloalkyl-(G)_m;
10 Substituted 3- to 6-membered heterocycloalkyl-(G)_m;
5- or 6-membered heteroaryl-(G)_m;
Substituted 5- or 6-membered heteroaryl-(G)_m;
 $(C_1-C_6 \text{ alkyl})-S(O)_2-N(H)-C(O)-(C_1-C_8 \text{ alkylene})_m$; and
 $(C_1-C_6 \text{ alkyl})-C(O)-N(H)-S(O)_2-(C_1-C_8 \text{ alkylene})_m$;
15 wherein each substituent on a carbon atom may further be independently selected from:
Halo; and
HO₂C;
wherein 2 substituents may be taken together with a carbon atom to which they
20 are both bonded to form the group C=O;
wherein two adjacent, substantially sp² carbon atoms may be taken together with a
diradical substituent to form a cyclic diradical selected from:





R is H or C₁-C₆ alkyl;

G is CH₂; O, S, S(O); or S(O)₂;

5 m is an integer of 0 or 1;

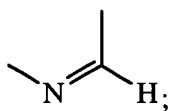
Y⁴, Y⁵, Y⁶, and Y⁸ are each independently C(R⁵) or N;

Y³ is C(O) or CH₂;

R⁴ and each R⁵ are each independently selected from the groups:

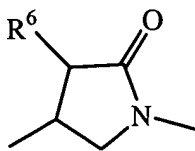
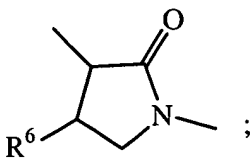
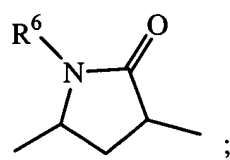
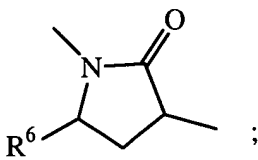
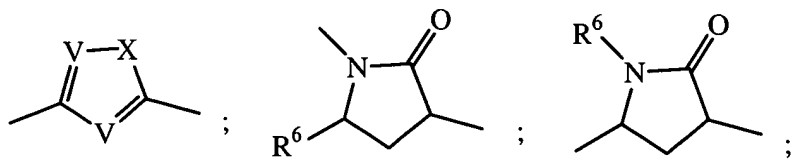
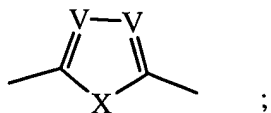
- H;
- 10 CH₃;
- CH₃O;
- CH=CH₂;
- HO;
- CF₃;
- 15 CN;
- HC(O);
- CH₃C(O);
- HC(NOH);
- H₂N;
- 20 (CH₃)-N(H);
- (CH₃)₂-N;
- H₂NC(O);
- (CH₃)-N(H)C(O); and
- (CH₃)₂-NC(O); or

25 R⁴ and Y³ may be taken together to form a diradical group:

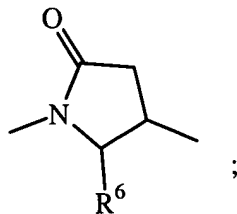


Q is selected from:

- OC(O);
 CH(R⁶)C(O);
 5 OC(NR⁶);
 CH(R⁶)C(NR⁶);
 N(R⁶)C(O);
 N(R⁶)C(S);
 N(R⁶)C(NR⁶);
 10 N(R⁶)CH₂;
 SC(O);
 CH(R⁶)C(S);
 SC(NR⁶);
 trans-(H)C=C(H);
 15 cis-(H)C=C(H);
 C≡C;
 CH₂C≡C;
 C≡CCH₂;
 CF₂C≡C; and
 20 C≡CCF₂;



; and



Each R⁶ independently is H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl; 3- to 6-membered heterocycloalkyl; phenyl; benzyl; or 5- or 6-membered heteroaryl;

X is O, S, N(H), or N(C₁-C₆ alkyl);

Each V is independently C(H) or N;

5 wherein each C₈-C₁₀ bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

10 wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 4 N(H), and 4 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double
15 bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 4 N(H), and 4 N(C₁-C₆ alkyl), and wherein when two O atoms or one O
20 atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms
25 and 1 or 2 heteroatoms independently selected from N, N(H), and N(C₁-C₆ alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N,
30 and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O

and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any (C₁-C₆ alkyl)₂-N group, the C₁-C₆ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and wherein each group and each substituent recited above is independently selected.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Y⁵, Y⁶, and Y⁸ are each C(R⁵), wherein each R⁵ is independently defined as above.

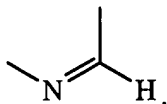
3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein one of Y⁵, Y⁶, and Y⁸ is N and the other two of Y⁵, Y⁶, and Y⁸ are each C(R⁵), wherein each R⁵ is independently defined as above.

4. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is N(R⁶)C(O).

5. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is C≡C.

6. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Y³ is C(O).

7. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Y³ and R⁴ is taken together to form a diradical group:



8. The compound according to any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein R¹ is independently selected from:

Phenyl-(C₁-C₈ alkylenyl);
Substituted phenyl-(C₁-C₈ alkylenyl);
5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
5 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl); and
Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl); and

R² is independently selected from:

Phenyl-(C₁-C₈ alkylenyl)_m;
Substituted phenyl-(C₁-C₈ alkylenyl)_m;
10 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl)_m;
Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl)_m;
8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl)_m; and
Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl)_m;

wherein m is an integer of 0 or 1; and

15 wherein each group and each substituent is independently selected.

9. The compound according to Claim 1, selected from:

3-(4-Methanesulfonyl-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-
quinazoline-6-carboxylic acid (pyridin-4-ylmethyl)-amide;
20 3-(4-Methanesulfonyl-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-
quinazoline-6-carboxylic acid (pyrimidin-5-ylmethyl)-amide;
3-(4-Methanesulfonyl-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-
quinazoline-6-carboxylic acid 4-methoxy-benzylamide;
3-(3-Chloro-4-fluoro-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-
25 quinazoline-6-carboxylic acid 4-methoxy-benzylamide;
4-[6-(4-Methoxy-benzylcarbamoyl)-1-methyl-2-oxo-1,4-dihydro-2H-
quinazolin-3-ylmethyl]-benzoic acid;
3-(4-Bromo-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-quinazoline-6-
carboxylic acid (pyridin-4-ylmethyl)-amide;
30 1-Methyl-3-(4-methylsulfonyl-benzyl)-2-oxo-1,2,3,4-tetrahydro-
quinazoline-6-carboxylic acid 3-methoxy-benzylamide;

- 3-(4-Methanesulfonyl-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-
pyrido[3,4-d]pyrimidine-6-carboxylic acid (pyridin-4-ylmethyl)-
amide;
- 5 3-(3-Chloro-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-pyrido[3,4-
d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-
amide;
- 3-(4-Cyano-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-pyrido[3,4-
d]pyrimidine-6-carboxylic acid (pyridin-4-ylmethyl)-amide;
- 10 4-[6-(4-Methoxy-benzylcarbamoyl)-1-methyl-2-oxo-1,4-dihydro-2H-
pyrido[3,4-d]pyrimidin-3-ylmethyl]-benzoic acid;
- 4-[6-(4-Methoxy-benzylcarbamoyl)-methyl-2-oxo-1,4-dihydro-2H-
pyrido[2,3-d]pyrimidin-3-ylmethyl]-benzoic acid;
- 1-Methyl-3-(4-methylsulfonyl-benzyl)-2-oxo-1,2,3,4-tetrahydro-
pyrido[2,3-d]pyrimidine-6-carboxylic acid (pyridin-3-ylmethyl)-
amide;
- 15 3-(4-Isopropyl-benzyl)-methyl-2-oxo-1,2,3,4-tetrahydro-pyrido[2,3-
d]pyrimidine-6-carboxylic acid (pyrimidin-5-ylmethyl)-amide;
- 1-Methyl-3-pyridin-3-ylmethyl-1,2,3,4-tetrahydro-quinazoline-6-
carboxylic acid 4-methyl-benzylamide;
- 20 {4-[6-Methoxy-benzylcarbamoyl)-1-methyl-1,4-dihydro-2H-pyrido[3,4-
d]pyrimidin-3-ylmethyl]-phenyl}-acetic acid;
- 3-Benzyl-1-methyl-1,2,3,4-tetrahydro-pyrido[2,3-d]pyrimidine-6-
carboxylic acid benzylamide;
- 3-Benzyl-3,4-dihydro-quinazoline-6-carboxylic acid 4-chloro-
benzylamide;
- 25 3-Benzyl-3,4-dihydro-pyrido[3,4-d]pyrimidine-6-carboxylic acid
(benzo[1,3]dioxo-5-ylmethyl)-amide; and
- 3-Benzyl-3,4-dihydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid 3-fluoro-
benzylamide;
- 30 or a pharmaceutically acceptable salt thereof.

10. The compound according to Claim 1, selected from:

- 3-(4-Methanesulfonyl-benzyl)-1-methyl-6-(3-phenyl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;
- 6-(3-Imidazol-1-yl-prop-1-ynyl)-3-(4-methanesulfonyl-benzyl)-1-methyl-3,4-dihydro-1H-quinazolin-2-one;
- 5 6-[3-(4-Fluoro-phenyl)-prop-1-ynyl]-3-(4-methanesulfonyl-benzyl)-1-methyl-3,4-dihydro-1H-quinazolin-2-one;
- 6-[3-(4-Chloro-phenyl)-prop-1-ynyl]-3-(4-methanesulfonyl-benzyl)-1-methyl-3,4-dihydro-1H-quinazolin-2-one;
- 10 3-(4-Methanesulfonyl-benzyl)-1-methyl-6-(3-pyridin-4-yl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;
- 3-(4-Methanesulfonyl-benzyl)-1-methyl-6-(4-phenyl-but-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;
- 3-(4-Methanesulfonyl-benzyl)-1-methyl-6-(3-naphthalen-2-yl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;
- 15 3-Benzyl-1-methyl-6-(3-phenyl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;
- 4-[1-Methyl-2-oxo-6-(3-phenyl-prop-1-ynyl)-1,4-dihydro-2H-quinazolin-3-ylmethyl]-benzoic acid;
- 3-(4-Chloro-benzyl)-1-methyl-6-(3-phenyl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;
- 20 3-(3,4-Difluoro-benzyl)-methyl-6-(3-phenyl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;
- 3-(4-Methoxy-benzyl)-1-methyl-6-(3-phenyl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;
- 25 4-[1-Methyl-2-oxo-6-(3-phenyl-prop-1-ynyl)-1,4-dihydro-2H-quinazolin-3-ylmethyl]-benzonitrile;
- 5-[1-Methyl-2-oxo-6-(3-phenyl-prop-1-ynyl)-1,4-dihydro-2H-quinazolin-3-ylmethyl]furan-2-carboxylic acid;
- 4-[1-Methyl-6-(3-methyl-3-phenyl-but-1-ynyl)-2-oxo-1,4-dihydro-2H-pyrido[2,3-d]pyrimidin-3-ylmethyl]benzoic acid;
- 30 3-Benzyl-1-methyl-6-(3-phenyl-prop-1-ynyl)-1,2,3,4-tetrahydro-pyrido[2,3-d]pyrimidine;

3-[6-(3-Phenyl-prop-1-ynyl)-4H-pyrido[2,3-d]pyrimidin-3-ylmethyl]benzonitrile; and

4-[6-(3,3-Difluoro-3-phenyl-prop-1-ynyl)-4H-quinazolin-3-ylmethyl]-benzoic acid;

5 or a pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

10

12. The pharmaceutical composition according to Claim 11, comprising a compound according to Claim 9 or 10, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

15

13. A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

20

14. The method according to Claim 11, wherein the compound administered is a compound according to Claim 9 or 10, or a pharmaceutically acceptable salt thereof.

25